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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,131	12/21/2001	Michael Leslie Kotewicz	0942.049000B/RWE/MTT	4058

26111 7590 07/22/2004

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,131	KOTEWICZ ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 20031117.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's Preliminary Amendment to the specification and the claims filed with the specification on December 21, 2001, introduces no new matter to the disclosure and the cancellation of claims 2-23 therein leaves only claim 1 pending for examination herein.

Information Disclosure Statements

Applicants' Information Disclosure Statements filed March 13, 2003 and November 17, 2003, and the documents and publications submitted therewith were considered. The PTO-Forms 1449 that accompanied these fifteenth, sixteenth and seventeenth information disclosures, were executed and attached to this communication. Applicant is invited to make of record herein the many other documents and publications cited in the recent re-examination applications sharing the disclosure of the instant application, less the publications cited on the PTO-Form 892 that accompanies this communication

Priority

While Applicant's Letter of Utility Patent Application transmittal identifies the instant application as a continuing application of the prior application serial No. 09/220,330, Applicant's Declaration of Inventorship states no claim to priority under 35 U.S.C. §120 to earlier-filed application(s). In addition, Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. §120 as follows: An application in which the benefits of earlier applications are desired must contain a specific reference to the prior applications in the first sentence of the specification and in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications and the current status of those applications, i.e, pending, abandoned, or issued as a patent.

Claim Objections

Claim 1 is objected to because of the following informalities: The claim lacks the presence of the indefinite article, "a", prior to "reverse transcriptase". Appropriate correction of this error in grammar is required.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

In the absence of a description that indicates either its isolation from Nature or its production by a person, claim 1 describes a gene that is still present in Nature, thus is drawn to a product of Nature which is not statutory subject matter.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,405,776. Although the conflicting claims are not identical, they are not patentably distinct from each other because the isolated DNA compounds of the patented claims all encode reverse transcriptases that substantially lack RNase H activity, thus share the properties required of the product encoded by the gene of claim 1 herein.

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,668,005. Although the conflicting claims are not identical, they are not patentably distinct from each other because the isolated DNA molecules of the patented claims all encode reverse transcriptases that substantially lack RNase H activity, thus share the properties required of the product encoded by the gene of claim 1 herein.

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 185 of U.S. Patent No. 6,063,608. Although the conflicting claims are not identical, they are not patentably distinct from each other because the isolated DNA molecules of the patented claim all encode reverse transcriptases that substantially lack RNase H activity, thus share the properties required of the product encoded by the gene of claim 1 herein.

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 151 of U.S. Patent No. 6,589,768. Although the conflicting claims are not identical, they are not patentably distinct from each other because the isolated DNA molecules of the multiply-dependent patented claim all encode reverse transcriptases that substantially lack RNase H activity, thus share the properties required of the product encoded by the gene of claim 1 herein.

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 85 of U.S. Patent No. 6,610,522. Although the conflicting claims are not identical, they are not patentably distinct from each other because the isolated DNA molecules of the patented claim all encode reverse transcriptases that substantially lack RNase H activity, thus share the properties required of the product encoded by the gene of claim 1 herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe the isolation of a naturally occurring gene of claim 1 or the preparation of any member of the broad genus of modified genes that the specification suggests are possible other than a modified retroviral reverse transcriptase gene, wherein the modification is a deletion of the region encoding the RNase H domain. The rejected claim reaches generic reverse transcriptase-encoding DNA segments that may specify products that need not have a source in retroviral genomes and reaches as well generic reverse transcriptase-encoding DNA segments lacking any modification of the native product's amino acid sequence or that have undisclosed modifications that result in the encoded product having "substantially no RNase H activity. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of reverse transcriptase genes from sources other than retroviral genomes, or of a retroviral reverse transcriptase gene that is not modified to delete a substantial portion of the region that encodes the RNase H domain, or that has a modification other than a deletion of the region encoding the RNase H domain. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of undisclosed genes form any source to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of the undisclosed genes of claim 1.

Claim 1 is rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for the preparation of a DNA molecule having a nucleotide sequence encoding a modified retroviral reverse transcriptase having DNA polymerase activity and reduced RNaseH activity wherein the modification is an amino acid sequence modification within the RNaseH domain producing reduced RNaseH activity,

does not reasonably provide enablement for recovering such a gene of claim 1 from Nature - because a retrovirus or a transposable element that possesses such a gene cannot persist - nor does it reasonably provide enablement for *de novo* design of a polynucleotide having a nucleic acid sequence encoding a RNA-dependent DNA polymerase having "substantially no" RNaseH activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is agreed that the specification and the prior art it cites, as well as the prior art cited in the prosecution histories of the parent applications - particularly the extensive teachings of the prior art made of record herein with Applicants' Information Disclosure which were discussed at length in the prosecution of the two precursor applications recently issued as U.S. Patents Nos. 6,063,608 and 6,610,522 - provide the artisan with sufficient guidance to recognize a retroviral reverse transcriptase gene. The scope of claim 1, which recites no limitation to a natural source for a reverse transcriptase-encoding nucleotide sequence, reaches reverse transcriptases produced by altering native, and non-native, DNA polymerase-encoding nucleotide sequences. No teaching in the prior art or in the instant specification permits the artisan to design a RNA-dependent DNA polymerase *de novo*. While the specification teaches how to inactivate, or greatly reduce, RNase H activity of a native retroviral reverse transcriptase by altering the RNaseH domain, specifically, by deleting all the codons in the nucleotide sequence within the region encoding the RNaseH domain, and optionally providing additional nucleotide sequences that encode stabilizing peptides at either terminus of a native coding region specifying the DNA polymerase, neither the specification nor the prior art teach how to modify a gene other than a retroviral reverse transcriptase gene to encode a RNA-dependent DNA polymerase having substantially no RNase H activity, nor how to modify a retroviral reverse transcriptase gene to encode a RNA-dependent

DNA polymerase having substantially no RNase H activity other than by altering it to produce a deletion of a substantial portion of the amino acid sequence within the RNase H domain that conserves the activity of the RNA-dependent DNA polymerase domain while crippling, or abolishing, the activity of the RNase H domain.

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Applying the enablement factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

> a) the specification lacks adequate, specific, guidance for altering genes other than a retroviral reverse transcriptase genes to produce a reverse transcriptase lacking RNase H activity, and lacks adequate, specific, guidance for altering a retroviral reverse transcriptase gene to produce a reverse transcriptase substantially lacking RNase H activity other than by deleting most or all of the codons in the region encoding the RNase H domain,
>
> b) the specification lacks working examples wherein genes encoding native reverse transcriptases having substantially no RNase H activity are isolated from any source and wherein genes other than retroviral reverse transcriptase genes are modified to produce a reverse transcriptase having the properties recited in claim 1,
>
> c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,
>
> d) unpredictability exists in the art where no other members of the broad class of reverse transcriptase genes have been modified to produce reverse transcriptases having substantially no RNase H activity except by codon modifications that inactivate the encoded RNase H domain.

Thus the scope of subject matter embraced by claim 1 is unsupported by the present specification even if taken in combination with teachings available in the prior art.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because the term "substantially no RNase H activity" is ambiguous where it is a relative description having no specific or particular measurement of what is, and what is not, "substantial".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
>
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Tanese and Goff, 1987, RNA Tumor Viruses, Cold Spring Harbor Laboratory, Pub. (Symposium, dates May 19-May 24, 1987), made of record herewith.

Absent a claim to priority in the Declaration of Inventorship executed by the co-inventors named herein and filed on December 21, 2001, and absent the perfection of a claim to priority by appropriate reference to prior applications upon which such a claim is made in the first sentence of the specification, the abstract of Tanese and Goff, disclosing a gene "which encodes [a] reverse transcriptase having DNA polymerase activity and substantially no RNase H activity", is available as prior art under 35 U.S.C. § 102(b), rather than 35 U.S.C. § 102(a) as it was applied in the prosecution of the application issuing as U.S. Patent No. 6,589,768, cited above.

Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Ankenbauer et al., EP 0 922 765, made of record herewith.

Absent a claim to priority in the Declaration of Inventorship executed by the co-inventors named herein and filed on December 21, 2001, and absent the perfection of a claim to priority by appropriate reference to prior applications upon which such a claim is made in the first sentence of the specification, Ankenbauer et al. is available as prior art. Ankenbauer et al. disclose, pages 7-9, Figure 1, and SEQ ID NO:10, a gene "which encodes [a] reverse transcriptase having DNA polymerase activity and substantially no RNase H activity."

Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Kacian et al., US 5,935,833, made of record herewith.

Absent a claim to priority in the Declaration of Inventorship executed by the co-inventors named herein and filed on December 21, 2001, and absent the perfection of a claim to priority by appropriate reference to prior applications upon which such a claim is made in the first sentence of the specification, Kacian et al. is available as prior art. Kacian et al. disclose, Examples 1-5 and 8-10 and Figures 8-10, the preparation of a "gene which encodes [a] reverse transcriptase having DNA polymerase activity and substantially no RNase H activity."

Claim 1 is rejected under 35 U.S.C. § 102(e)(1) as being anticipated by Smith et al., US 2002/0090618, made of record herewith.

Absent a claim to priority in the Declaration of Inventorship executed by the co-inventors named herein and filed on December 21, 2001, and absent the perfection of a claim to priority by appropriate reference to prior applications upon which such a claim is made in the first sentence of the specification, Smith et al. is available as prior art in view of their May 26, 2000, provisional application priority date. Smith et al. disclose, paragraphs 223-228 and Table 3, the preparation of a gene "which encodes [a] reverse transcriptase having DNA polymerase activity and substantially no RNase H activity."

Claim 1 is rejected under 35 U.S.C. § 102(e)(1) as being anticipated by Potter et al., US 2003/0003452, made of record herewith.

Absent a claim to priority in the Declaration of Inventorship executed by the co-inventors named herein and filed on December 21, 2001, and absent the perfection of a claim to priority by appropriate reference to prior applications upon which such a claim is made in the first sentence of the specification, Potter et al. is available as prior art in view of their March 15, 2000, provisional application priority date. Potter et al. disclose, paragraphs 157-186 and Table 3, the preparation of a gene "which encodes [a] reverse transcriptase having DNA polymerase activity and substantially no RNase H activity."

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone numbers for all communications for the organization where this application or proceeding is assigned remains 703.872.9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore
July 12, 2004